REMARKS

Claims 1-23 are pending in the above-identified application. By the present amendment claims 12 and 22 have been cancelled and claims 1, 13, 17, and 19-21 have been amended. Claim 1 has been amended to be directed to determining or predicting the risk of the recurrence of colorectal cancer, support for which can be found in the specification including, for example, on page 10, line 4, through page 11, line 8 and page 14, lines 13-23. Claims 13, 19 and 20 have been amended to be directed to determining the likelihood that colorectal cancer will become metastatic, wherein chromosome 6 gains or chromosome 4 losses are prognostic of metastasis. Support for the amendments to claims 13, 19 and 20 can be found in the specification including, for example, on page 14, lines 13-24 and page 23, lines 8-26. Claim 17 has been amended to be directed to prognosing survival wherein chromosome 4 loss is prognostic of poor survival, support for which can be found in the specification including, for example, on page 24, line 22, through page 25, line 13. Claim 21 has been amended to recite colorectal cancer, support for which can be found in the specification including, for example, on page 25, line 14, through page 26, line 9 and page 6, line 9, through page 7, line 3. Claims 1, 13, 17, 19 and 21 have also been amended to correct obvious errors.

As set forth above, the amendments do not introduce new matter. Furthermore, Applicant respectfully submits that entry of the amendments after final is proper because the amendments

cancel claims, place the claims into condition for allowance or in better form for consideration on appeal, and do not raise new issues for consideration in accordance with 37 CFR 1.116 and MPEP 714.12 and 714.13. Therefore, entry of the amendments is respectfully requested. A marked-up copy of the claims showing the amendments is attached hereto as Appendix A.

Applicants respectfully traverse the rejection of claims 1-23 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification commensurate with the scope of the claims. Applicants maintain, for the reasons of record that the specification is enabling for claims 1-23. Nevertheless, in order to further prosecution of this application, claims 12 and 22 have been cancelled and claims 1, 13, 17, and 19-21 have been amended.

Following entry of the amendments, Claim 1 will be directed to determining or predicting the risk of the recurrence of colorectal cancer using a Genomic Damage Fraction. As taught on page 13, lines 10-17 of the specification the term "Genomic Damage Fraction" refers to a measure of the change in quantity of nucleic acids between cancerous cells and normal cells in an individual. Thus, Applicants respectfully submit that following entry of the amendments, claims 1-12 will be in accordance with the subject matter which the Office Action asserts to be enabled, in stating on page 2, lines 10-14, that the specification, is enabling for a method of determining an increased or decreased risk of developing colorectal cancer by determining the relative

change in the quantity of nucleic acids between cancerous and noncancerous cells.

Following entry of the amendments, claims 13, 19 and 20 will be directed to determining the likelihood that colorectal cancer will become metastatic, wherein chromosome 6 gains or chromosome 4 losses are prognostic of metastasis. As acknowledged on page 5, lines 14-17 of the Office Action, the specification teaches that chromosome 4 losses and chromosome 6 gains were significantly associated to the metastatic stage (see page 23, lines 8-26 and Figure 6). Thus, Applicants respectfully submit that following entry of the amendments, claims 13-16, 19 and 20 will be in accordance with the subject matter which the Office Action asserts to be enabled.

Following entry of the amendments, claim 17 will be directed to prognosing survival, wherein chromosome 4 loss is prognostic of poor survival. As acknowledged on page 5, lines 17-20 of the Office Action, the specification teaches that loss in chromosome 4 was a prognostic indicator of poor survival (see page 25, line 22, through page 25, line 13 and Figure 7). Thus, Applicants respectfully submit that following entry of the amendments, claims 17 and 18 will be in accordance with the subject matter which the Office Action asserts to be enabled.

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-23 under 35 U.S.C. § 112, first paragraph, be removed.

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned agent or Cathryn Campbell.

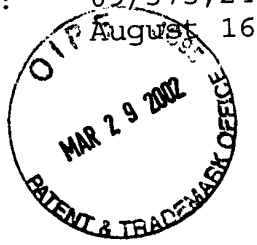
Respectfully submitted,

March 22, 2002
Date

John T. Murphy
Registration No. 50,583
Telephone No. (858) 535-9001
Facsimile No. (858) 535-8949

CAMPBELL & FLORES LLP
4370 La Jolla Village Drive
7th Floor
San Diego, California 92122
USPTO CUSTOMER NO. 23601

Inventors: Perucho and Malkhosyan
Serial No.: 09/375,246
Filed: August 16, 1999



APPENDIX A

Marked-up version of claims showing amendments.

1. (Amended) A method of determining the risk of the recurrence of colorectal cancer for [clinical outcome of] a subject [with a cancer] using a Genomic Damage Fraction, comprising: [,]

a. determining the relative change in quantity of nucleic acids between cancerous cells and non-cancerous cells of said subject;

b. determining the Genomic Damage Fraction from the results of step (a)

c. determining the prognosis of said subject according to said subject's GDF, where a GDF greater than a predetermined GDF is indicative of a first clinical outcome, and a GDF lesser than a predetermined GDF is indicative of a second clinical outcome, wherein said clinical outcome comprises risk of the recurrence of colorectal cancer.

13. (Amended) A method of determining the likelihood that colorectal cancer will become metastatic for [clinical outcome of] a subject with colorectal [a] cancer, comprising: [,]

a. generating the AP-PCR DNA fingerprint of non-cancerous cells from said subject;

b. generating the AP-PCR DNA fingerprint of primary cancer cells from said subject;

[c. generating the AP-PCR DNA fingerprint of metastatic cancer cells from said subject;] and

c [d]. identifying chromosomal regions from AP-PCR DNA fingerprint data of steps (a), (b) and (c) wherein the occurrence of chromosome 6 gains or chromosome 4 losses [of nucleic acids in certain chromosomal regions] is prognostic of metastasis [the clinical outcome] for said colorectal cancer [subject].

17. (Amended) A method of prognosing survival for [determining the clinical outcome of] a subject with colorectal [a] cancer, comprising: [,]

a. generating the AP-PCR DNA fingerprint of non-cancerous cells from said subject;

b. generating the AP-PCR DNA fingerprint of primary cancer cells from said subject;

c. identifying chromosomal regions from AP-PCR DNA fingerprint data of steps (a) and (b), where gains or losses of nucleic acids occur; and

d. comparing said AP-PCR DNA fingerprints [of chromosomes 1, 4, 6, 8, 9, and 13] from step a and step b wherein [presence of gain or] chromosome 4 loss [of nucleic acids in certain chromosomal regions] is prognostic of poor survival [the clinical outcome] for said subject.

19. (Amended) A method of predicting the likelihood that colorectal cancer will become metastatic for [a clinical outcome of] a subject with colorectal [a] cancer using an amplotype from said subject, comprising: [,]

a. locating chromosomal regions that have gained and lost nucleic acids using AP-PCR DNA fingerprinting;

b. identifying said chromosomal regions that have lost nucleic acids; and

c. identifying said chromosomal regions that have gained nucleic acids;

wherein the combination of chromosome 6 gains and chromosome 4 losses [according to chromosomal regions] are prognostic of metastasis [the clinical outcome] for said colorectal [subject with] cancer.

20. (Amended) The method of claim 19, wherein the results of step (b) and step (c) are displayed where said gains and losses of nucleic acids are listed according to the chromosomal regions where they occur, wherein the combination of gains and losses according to chromosomal regions are prognostic of metastasis [the clinical outcome] for said colorectal [subject with] cancer.

21. (Amended) A method of identifying a genomic region relevant for colorectal [a] cancer in a subject having colorectal [said] cancer, comprising: [,]

(a) generating the AP-PCR DNA fingerprint of non-cancerous cells, primary cancer, and metastatic tumor cells from said subject; and

(b) identifying said genomic regions from AP-PCR DNA fingerprint data of step (a), showing gains and losses of nucleic acids in [is] certain genomic regions, thereby identifying a genomic region linked to a colorectal cancer gene.